

# Cystitis and its management

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## Educational aims

- To provide an overview of urinary tract infections and cystitis, underlying the difference between the latter and interstitial cystitis
- To outline the major causes of cystitis and the signs and symptoms that are associated with it
- To describe the different tests that are used to diagnose an episode of cystitis
- To highlight the various classes of medications that are used to prevent and treat cystitis
- To offer a series of recommendations for lifestyle modifications that will help prevent further episodes

## Key words

urinary tract infection, cystitis, dipstick test, alkalinising agents, antibiotics, probiotics, cranberry juice

## Abstract

**Urinary tract infections are very common. They are responsible for over 6 million patient visits to doctors per year in the United States.<sup>1</sup> These include over 2 million cases that are attributed to cystitis which is the most common urinary tract infection. Cystitis can be defined as an inflammation of the bladder and it may result in pain and discomfort. Women tend to suffer from this condition more than men, although the chance of men acquiring cystitis increases with age. Untreated cystitis can lead to kidney infection, even kidney damage. Treatment for cystitis ranges from over-the-counter medications to antibiotics if the cause is an infection.<sup>2</sup>**

## Introduction

Urinary tract infections (UTIs) are divided into lower and upper tract infections. Lower UTIs (LUTIs) include the bladder and urethra, whereas upper UTIs involve the kidneys. Many a time, the infection migrates from one part of the tract to another. Most UTIs are caused by bacteria, although sexually transmitted pathogens, mycobacteria, fungi and parasites also give rise to such infections.<sup>3</sup>

Bacterial UTIs involve any part of the urinary tract and may be asymptomatic or characterized by the symptoms that are normally associated with these infections. Diagnosis focuses on the doctor taking a detailed history of the presenting complaints by the patient, together with a urine analysis and urine culture. Treatment usually involves the use of antibiotics. When considering adults up to 50 years of age, bacterial UTIs are much more common in females. The incidence of these infections increases in both male and female patients over 50 years of age. On the other hand, the female:male ratio decreases, a reason being an increased frequency of prostate disease.<sup>3</sup>

The urinary tract is normally a sterile environment and this is very often maintained due to various reasons which may include the acidity of the urine, emptying of the bladder at micturition and various immunological and mucosal barriers. Most UTIs occur when the pathogenic bacteria ascend the urethra to the bladder.<sup>3</sup> A bacterial infection of the urethra, urethritis, is mainly caused by the sexually transmitted pathogens, *Chlamydia trachomatis*, and *Neisseria gonorrhoea*.<sup>1</sup>

Cystitis is the term used to describe a bladder inflammation that is very often due to an infection which is usually of bacterial origin. Examples of such micro-organisms include *Escherichia coli* (70-95% of all cases) and *Klebsiella pneumonia*. A bladder infection may become a serious health problem if not treated, as the infection will otherwise spread to the kidneys. This may result in renal failure or pyelonephritis.<sup>3</sup> Due to complications of cystitis, mortality rates can be as high as 1% in men and 3% in women.<sup>1</sup>

Non-infective episodes of cystitis are rare and they may be due to:<sup>1</sup>

- radiation therapy
- certain medicines such as cyclophosphamide; this is thought to be due to the metabolites that are excreted in the urine - effects appear to be

**Table 1: Typical signs and symptoms of cystitis**

- A strong, persistent urge to urinate
- Haematuria
- Dysuria
- Lower back and/or abdominal pain and discomfort
- Fever
- Malaise
- Pressure in lower pelvis

related to the dose of medication taken and to the duration of therapy

- the long-term use of a catheter
- hypersensitivity to certain chemicals that can be found in spermicidal gels, feminine hygiene sprays and shower gels or bath foams.

Interstitial cystitis (IC), also known as painful bladder syndrome, should not be confused with cystitis. IC is a chronic bladder inflammation that is not bacterial in origin. It affects both sexes and known causes are sexual intercourse, mental and/or physical stress and menses in women. IC may occur in association with other conditions, such as sinusitis, hay fever, fibromyalgia, migraines and food allergies.<sup>4</sup> Treatment does not involve antibiotics but requires personalized detailed patient education. Patients must be well informed on potential trigger factors. This will help patients enjoy long periods of remission and a better quality of life.

#### Risk factors

Cystitis commonly occurs in females; about 20% of women, sooner or later, develop a UTI.<sup>5</sup> This is mainly due to women having a shorter urethra than men. Women aged 18-30 years are very prone to getting cystitis; sexually active females are at a greater risk of developing cystitis as sexual intercourse can result in bacteria being pushed into the urethra. Hormonal changes that occur in pregnancy and the use of diaphragms also attribute to an increased risk of cystitis. Altered hormonal levels in postmenopausal women and a bladder or uterine prolapse may cause incomplete bladder emptying are also associated with cystitis.<sup>1</sup> Cystitis may also arise as a complication of another illness, an example being diabetes.

On the other hand, cystitis is quite rare in younger men and children. Whenever a man presents with symptoms pertaining to cystitis he should be immediately referred to a doctor as the symptoms may be indicative of an underlying pathology, such as stones in

the bladder or an enlarged prostate.<sup>2</sup>

Children are very susceptible to kidney and bladder damage as a result of a urinary tract infection. A UTI in children may be an indication of structural abnormalities within the urinary tract and it hence merits further investigations by a urologist.

#### Signs and symptoms

The symptoms of cystitis are very similar to the ones an individual experiences when suffering from acute urethritis that arises due to sexually transmitted diseases.<sup>3</sup> The symptoms of vaginitis are also very similar to those of cystitis, although the former is often characterized by the presence of vaginal odour, dyspareunia and vaginal discharge.<sup>5</sup> It is thus of major importance that other conditions are ruled out before treating an individual for cystitis.

Typical signs and symptoms pertaining to cystitis are presented in Table 1.

Catheterised and elderly patients may present with atypical symptoms which will unfortunately delay a correct diagnosis and hence the appropriate treatment to be given.<sup>6</sup> Such atypical symptoms are presented in Table 2.

#### Diagnosis

Various diagnostic studies confirm cystitis. These include a urine dipstick test, urinalysis and a bacterial culture. Imaging studies are not indicated in the routine evaluation of cystitis.<sup>5</sup> A dipstick test is usually sufficient to diagnose an episode of cystitis. This may be performed by a pharmacist or doctor and is very cost-effective and convenient to carry

out. Ideally, a mid-stream urine is used to perform the test to remove the commensal flora in order to avoid contamination.<sup>7</sup>

The dipstick test may result in microscopic haematuria, proteinuria, a positive nitrate test and a positive leukocyte esterase test. These are all indicative of a UTI. The most accurate indicators - 98% - of an acute uncomplicated episode of cystitis in symptomatic individuals are the presence of nitrites and leukocyte esterase in the urine sample.<sup>7</sup> According to the guidelines issued by the local National Antibiotic Committee for antibiotic use in LUTIs in the community setting, a negative dipstick test excludes a UTI, including cystitis. On the other hand, a positive test does not necessarily confirm a UTI but the presence of leukocyte esterase and nitrites may indicate the presence of a UTI.<sup>8</sup>

The dipstick test makes use of the Kastle-Meyer test which detects the peroxidase activity of red blood cells. In this test, the chemical indicator, phenolphthalein is used to detect the possible presence of haemoglobin. Haemoglobin catalyses the oxidation of the colourless reduced form of phenolphthalein into phenolphthalein. The latter is visible as a bright violet colour. False-positive results may result due to a contaminated specimen container or due to the presence of semen in the urine. Blood in the urine may also be due to vaginal bleeding or bleeding haemorrhoids.<sup>7</sup> The detection of haematuria can therefore give rise to a high rate of false positives and also false negatives. For this reason, this test is unreliable and cannot be considered in isolation.<sup>7</sup>

Normal urine contains very little protein which consists mainly of low-molecular-weight serum proteins that have been filtered by the glomerulus and proteins that are produced in the genitourinary tract. The albumin content of urine is normally low because most of this protein is not filtered at the glomerulus. A large amount

**Table 2: Atypical signs and symptoms of cystitis**

- Abdominal pain
- Nausea and vomiting
- Urinary retention
- Altered mental state
- Worsening in the control of diabetes
- Rigors
- New-onset incontinence

of any filtered albumin is reabsorbed by the tubules. Other proteins found in urine may include small amounts of tubular microglobulins. The urinary dipstick test only detects the presence of albumin. A negative protein result therefore does not rule out the presence of globulins. This test is therefore also unreliable and of little diagnostic value.<sup>7</sup>

The urine dipstick test to check for proteinuria is based on the fact that certain indicators vary in colour in the presence of protein even though the pH of the medium remains the same. This occurs because proteins tend to accept hydrogen ions from the indicator on the test strip. The dipstick test is very sensitive to albumin because albumin contains more amino groups than other proteins. For this reason, albumin can accept more hydrogen ions. Indicators appear yellow in the absence of protein but as the protein concentration increases, the colour change progresses through various shades of green.<sup>7</sup>

Nitrites are not normally present in the urine. They are produced when Gram negative bacteria, examples being *Escherichia coli*, *Enterobacter* and *Klebsiella* reduce dietary nitrates to nitrites. In order for the nitrate test to be reliable, the urine specimen should be one that has been present in the bladder for at least four hours so that sufficient time elapses for the nitrate to nitrite conversion to take place. Negative results in the presence of clinical symptoms can be obtained and this may be due to the presence of non nitrate-reducing micro-organisms. Also, some bacteria can convert nitrite to nitrogen and this too will give a false negative result.<sup>7</sup>

White blood cells contain an enzyme called leukocyte esterase. This is released when the white blood cells undergo lysis. Very few white blood cells are usually present in the urine for the dipstick test to be positive. However, when there is a large number of white blood cells present in the urine, as in the case of a UTI, a positive result is obtained. The reaction that takes place is based on the fact that the leukocyte esterase catalyses the hydrolysis of an ester of indolecarboxylic acid on the reagent strip. As a result, the indoxyl that is liberated combines with a diazonium salt. A violet coloured azole dye is subsequently obtained.<sup>7</sup>

Urine microscopy may be necessary if the dipstick test is negative and the patients are experiencing the clinical symptoms that are normally associated with cystitis. Some patients - immunosuppressed

patients, pregnant women, children under three years of age, individuals who have recurrent UTIs, those who have had a recent urinary tract intervention and those who are of an advanced age - who experience the symptoms of cystitis must be subject to a urine culture test at all costs as the dipstick test is considered to be unreliable.<sup>1,7</sup> Bacterial culture is not usually necessary to confirm the diagnosis of an episode of cystitis in a non-pregnant woman. If however she does not respond to first-line treatment, her urine should be cultured so that the appropriate medication will be prescribed.<sup>7</sup>

Microscopy is used to determine haematuria, bacteriuria and pyuria. Haematuria is not always present in cystitis and it can also be associated with other conditions, an example being neoplasia. Bacteriuria, especially with pyuria, highly suggests an infection whereas pyuria occurring in isolation is an indicator of a urinary tract inflammation; it however does not confirm the presence of an infection.<sup>7</sup>

#### Treatment

Pharmacotherapy in cystitis aims to:

- provide symptomatic relief to the patients
- eradicate the infection
- prevent complications - early treatment is recommended to reduce the risk of complications.

The diagnosis and management of uncomplicated acute episodes of cystitis are relatively straightforward to handle. On the other hand, recurrent and complicated infections require more specialized assessment. Without any treatment, 25-42% of uncomplicated episodes of cystitis in women will resolve spontaneously. The chance of these women developing pyelonephritis is around 2%.<sup>5</sup>

The treatment for cystitis varies as it depends on the underlying cause. Cystitis that occurs because of radiation therapy involves adequate hydration to flush out any irritants and also pain management. For chemical cystitis it is recommended to discontinue the use of the irritating products.

At times, it is impossible for some patients to visit their doctors. Studies have demonstrated that there may be incidences when women who self-diagnose a UTI are treated safely via telephone management.<sup>5</sup> Women who have previously suffered from

acute uncomplicated cystitis are usually correct in determining when they are suffering from another episode.

#### Paracetamol and Non-steroidal anti-inflammatory drugs (NSAIDs)

These medications act as antipyretics and also reduce the pain or discomfort experienced by the patient. NSAIDs reduce the production of prostaglandins by inhibiting cyclo-oxygenase. They vary in their selectivity for inhibiting the different types of cyclo-oxygenase; the NSAIDs that are selective cyclo-oxygenase-2 inhibitors, such examples being etoricoxib and celecoxib, are associated with less gastrointestinal intolerance. They hence reduce the risk of peptic ulceration. In the elderly and other high risk patients, the use of a proton pump inhibitor (PPI) is highly recommended together with the cyclo-oxygenase-2 inhibitor. It is of utmost importance that on dispensing, the pharmacist informs the patient to take the NSAIDs after food in order to further reduce gastrointestinal upset. On the other hand, the PPI is ideally taken one hour before breakfast.

#### Alkalinising agents

Alkalinising agents include sodium bicarbonate, sodium citrate, potassium citrate and sodium carbonate. Although there is no clinical evidence to support their use, sources claim that they actually relieve discomfort.<sup>2</sup>

The recommended dosage for the preparations that are available locally is one sachet three times a day for two days. If the symptoms do not subside, patients ought to be referred to a doctor as further investigations and/or antibiotic therapy may be required.

Since the sodium content in the sachets is relatively high, these preparations should be avoided in individuals who are on a diet that requires a restricted salt intake. They should also be avoided in hypertensive patients as they will cause fluid retention and further increase the blood pressure. Diabetics, pregnant women, patients who have heart disease and/or renal failure should also avoid these products as these patients, as previously noted, should be referred immediately.<sup>2</sup> It is of major importance that patients who are on lithium therapy should not be given these sachets because sodium is preferentially absorbed by the kidney. Lithium excretion is hence

**Table 3: Maltese guidelines to treat UTIs in the community**

UTI in pregnancy	First line: nitrofurantoin Amoxicillin if organism is sensitive	50-100mg qds x 7 days 500mg tds x 7 days
UTI in children	Second line: cephalexin LUTI: coamoxiclav	500mg tds x 7 days 15mg/kg/dose tds x 3 days
LUTI in men and women (no fever)	Second line: cefuroxime If pH< 7: nitrofurantoin If pH>7: coamoxiclav	10-15mg/kg/dose bd x 3 days 50-100mg qds; female x 3 days and males x 7 days 625mg tds; female x 3 days and males x 7 days

increased thus resulting in reduced plasma concentrations.<sup>9</sup>

These sachets must also be used with caution in patients who are on medications that require an acidic urine to be excreted.<sup>10</sup> Patients taking certain medications that increase the potassium level, such as potassium sparing diuretics, aldosterone antagonists and angiotensin converting enzyme inhibitors, should consult the doctor before taking the potassium-salt containing sachets because of the risk of hyperkalaemia.<sup>2</sup>

#### **D-Mannose**

According to The National Institute for Health and Care Excellence Guidelines, D-Mannose is the most effective over-the-counter supplement for preventing and treating urinary tract infections. Similar to glucose in structure, D-mannose is a naturally occurring sugar and can be found in several fruits such as apples, blueberries, and cranberries. D-mannose is effective because it attaches itself to *Escherichia coli* and as a result, the bacteria are eliminated from the body during micturition. Even if taken in large quantities, D-mannose does not cause any adverse effects. It is safe in diabetics and can be easily taken by patients who have to avoid sugar.<sup>11</sup> The preparation that is available locally should be taken twice daily for a week and ideally should be continued even after the infection subsides so as to ensure complete elimination of the bacteria in the urinary tract. Individuals who are prone to recurrent urinary tract infections can take D-mannose on a regular basis as a means of prevention.

#### **Antibiotics**

According to the 2010 Infectious Diseases Society of America (IDSA) guidelines, no antibiotic is considered as being ideal for treating acute uncomplicated episodes of cystitis. The choice of antibiotic depends on several factors and these include the medication's efficacy, any associated adverse

side effects and the resistance the microorganisms exhibit.<sup>5</sup> The prevalence of antibiotic-resistant infections tends to be higher in patients who suffer from recurrent infections and who have taken various antibiotics due to other illnesses. Physicians should also consider ease of availability, cost and individual patient factors, such as a history of allergy. Although published guidelines offer choices for the various antibiotics that can be prescribed by doctors, studies have shown that prescribing practices vary tremendously.

Since most cases of cystitis are caused by *Escherichia coli*, it is of major importance that this microbe is not resistant to the antibiotic that is chosen for empirical treatment. The resistance patterns of *Escherichia coli* vary considerably between countries. A specific recommended treatment protocol may therefore not be suitable for all regions.<sup>12</sup>

According to the IDSA guidelines, the antibiotics that are to be considered as the treatment of choice for uncomplicated and acute episodes of cystitis in women include nitrofurantoin or trimethoprim-sulfamethoxazole or fosfomycin. Fluoroquinolones are usually used to treat complicated episodes of cystitis and should not be used as a first line for the empirical treatment of LUTIs. Their use should be guided by culture and sensitivity results. Beta-lactam antibiotics may be prescribed when other recommended medications cannot be used. For instance, fosfomycin and nitrofurantoin should be avoided in patients who suffer from a possible early episode of pyelonephritis.<sup>5</sup>

The Maltese National Antibiotic Committee issued treatment guidelines for the treatment of UTIs in the community.<sup>8</sup> These are presented in Table 3.

The local guidelines stipulate that in women and children, a three day course of antibiotics is usually sufficient to cure an

uncomplicated acute case of cystitis whereas males and pregnant women should be treated for at least 7 days. Children suffering from upper UTIs should also be treated for 7 to 10 days.<sup>8</sup>

It is clearly shown that the local guidelines differ from the 2010 IDSA guidelines. Co-trimoxazole, for example is presently no longer indicated for the empirical treatment of LUTIs. This contrasts with the local widespread use of this drug over twenty years ago.

Pharmacists are in a key position in advising the patient on the proper administration of the medication. It is to be noted that on average, patients will begin experiencing symptom relief within 36 hours of commencing the treatment. The whole course of antibiotics must be taken even if the patient feels better before completion.

#### **Nitrofurantoin monohydrate**

Nitrofurantoin is highly effective against *Escherichia coli*, many Gram negative bacteria and Gram positive cocci. The duration of therapy for nitrofurantoin has been reduced to five days in the 2010 IDSA guidelines. This varies from the stipulated seven day treatment recommended in the previous 1999 guidelines.<sup>5</sup> Nitrofurantoin is generally well tolerated, with no significant effects on vaginal flora. It is contraindicated in patient with impaired renal function and possible adverse effects include nausea, vomiting, hypersensitivity, peripheral neuropathy, hepatitis and haemolytic anaemia.<sup>9</sup> Nitrofurantoin lacks significant drug interactions although administration with alkalisating agents renders the antimicrobial ineffective due to the alkaline pH. The pharmacist should advise the patient to take the medication with food and not to get alarmed if the urine is coloured yellow or brown. Nitrofurantoin is unlikely to cause problems to the foetus if given for a short period in pregnancy. It however cannot be given at term or during breastfeeding.

### **Trimethoprim–sulfamethoxazole**

These two antibiotics are used in combination due to their synergistic activity. They interfere with two consecutive steps in the biosynthesis of nucleic acids and proteins that are essential to many bacteria.<sup>5</sup> Trimethoprim inhibits dihydrofolate reductase; the synthesis of tetrahydrofolic acid from dihydrofolic acid is therefore inhibited. Sulfamethoxazole, on the other hand, inhibits the synthesis of dihydrofolic acid by competing with para-aminobenzoic acid. Co-trimoxazole should not be prescribed to individuals who have already taken it in the previous three months for cystitis. This antibiotic has been associated with rare, but serious adverse effects which include Stevens-Johnson syndrome, photosensitivity reactions and blood dyscrasias. More common adverse effects include diarrhoea, nausea and headache.<sup>9</sup> The pharmacist ought to advise the patient regarding adequate fluid intake whilst taking the antibiotic and to also avoid direct sunlight. Patients taking warfarin should not be prescribed co-trimoxazole because of the increased anticoagulant effect due to trimethoprim.<sup>9</sup> There is also an increased risk of hyperkalaemia when trimethoprim is given with angiotensin converting enzyme inhibitors or angiotensin II receptor antagonists.<sup>9</sup>

### **Fosfomycin tromethamine**

In the United States fosfomycin is not widely available because it is considered to be less effective than standard short-course regimens. This antibiotic inhibits bacterial cell wall synthesis and also reduces bacterial adherence to the urinary tract. Adverse effects may include diarrhoea, nausea, vomiting, drowsiness and pruritus.<sup>5</sup> The pharmacist should advise the patient to add the sachet contents to a glass of cold water, to stir it and drink it straight away, ideally in the evening, with or without food. Symptoms should improve within two to three days after taking the medication; if symptoms persist or worsen, the doctor must be contacted. It is very important to inform the patient not to use more than one sachet as more packets will not make the medication work better. On the other hand, adverse effects will be increased. It would be very useful to limit the local use of this new medication because fosfomycin is active against most local multidrug resistant strains of Gram negative organisms. It will therefore save on the use of second line antibiotics, such as carbapenems within the hospital setting.

### **Quinolones**

Quinolones are very effective against Gram negative bacteria and to a lesser extent also inhibit Gram positive bacteria. Unfortunately, resistance to quinolones is on the increase.<sup>5</sup> The use of low dose ciprofloxacin is replacing older quinolones (norfloxacin) due to the former's better pharmacokinetic properties. Quinolones should be used with caution in patients who have a history of epilepsy since a main adverse effect is that they may induce convulsions. Other adverse effects may include rash, headache, restlessness, an Achilles tendon rupture especially in patients who are older than 60 years and a QT interval prolongation. The community pharmacist should advise the patient to take the medications after food and to avoid direct sunlight due to photosensitivity reactions. Dairy products should not be taken with quinolones as the absorption of the medication will be reduced. Very important interactions involving quinolones include those with warfarin – where the anticoagulant effect is enhanced – and NSAIDs – where the risk of convulsions is increased if they are given concomitantly.<sup>9</sup> Also, ciprofloxacin should not be given with calcium supplements and alkalinising agents due to the risk of chelation and crystalluria respectively.

### **Beta-lactam antibiotics**

Cephalosporins are rarely indicated for LUTIs because of increased resistance by Gram negative bacteria. Amoxicillin should be avoided as much as possible because resistance to this agent is also very high. Beta-lactam antibiotics tend to have inferior efficacy and more associated adverse effects than nitrofurantoin.<sup>5</sup> They therefore should be used with extreme caution in uncomplicated cases of cystitis. The pharmacist should advise the patient regarding possible adverse effects which can be avoided; the individual should take probiotics with the antibiotic so as to prevent diarrhoea and use an intimate wash to help avoid vaginal candidiasis.

Women who suffer from more than three recurrent UTIs a year should take prophylactic antibiotics in addition to behavioural modification. Women whose recurrent UTIs are associated with sexual intercourse should take a single dose of an effective antibiotic as post-coital prophylaxis.<sup>5</sup> Local guidelines recommend a 50mg nitrofurantoin STAT dose. Prophylactic antibiotic use should not be taken for

more than six to twelve months due to the risk of bacterial resistance and also due to the occurrence of adverse effects, such as gastrointestinal effects and rashes.<sup>10,13</sup> Patients should be well informed about the fact that the antibiotic prophylaxis is not usually a life-long treatment. The medication, however, is to be taken for the required period of time so as to allow adequate healing of the bladder to take place and it should ideally be taken at night when urine flow is rather low.<sup>10</sup> Men and patients who have an indwelling catheter should not take a daily dose of prophylactic antibiotic therapy unless the medications are prescribed by a urologist, microbiologist or nephrologist.<sup>14</sup>

### **Probiotics**

Probiotics can be defined as, "live microorganisms, which when administered in adequate amounts confer a health benefit on the host".<sup>15</sup> The micro-organisms that inhabit the vaginal tract play a very important role in the prevention of infections and also in the maintenance of good health. About 50 different types of microbial species inhabit the vagina. The species that are present in the vaginal mucosa vary between premenopausal and postmenopausal women. The microbial flora of a healthy premenopausal woman is normally dominated by the *Lactobacillus* species. Various factors such as hormonal changes (especially in oestrogen levels) and vaginal pH can affect the colonization of the *Lactobacilli* in the vagina. Spermicides for example, lead to a loss of *Lactobacilli* and alter the pH.<sup>15</sup> The growth of Gram-negative organisms is therefore stimulated, thus resulting in cystitis.

*Lactobacilli* are required in the vaginal mucosa for various reasons - they produce antibacterial materials, an example being hydrogen peroxide, so as to limit pathogen growth. They also produce biosurfactants that inhibit pathogen adherence to the mucosa and attract macrophages, leucocytes and other host defences to the particular area.<sup>15</sup>

Clinical trials have demonstrated that a number of strains of *Lactobacilli* are very effective at helping to treat and prevent cystitis. Taking *Lactobacillus* probiotics daily as prevention for cystitis offers advantages over long term preventive antibiotic therapy; probiotics do not cause antibiotic resistance and unlike antibiotics allow re-colonization of bacteria to take place.<sup>15</sup>

### Cranberry oral preparations

The mechanism of action of cranberries as a prevention of cystitis has not been fully understood. Cranberries contain water (as their main constituent) and carbohydrates. Benzoic acid in cranberry juice is excreted in urine as hippuric acid which is a bacteriostatic agent; it has the potential to acidify urine. Studies have also shown that in petri dishes, cranberry metabolites prevent *Escherichia coli* from adhering to other bacteria, hence limiting its ability to grow and multiply.<sup>10,16</sup> Despite this, results of studies are rather inconsistent and the required dose to be taken is unclear.<sup>10</sup> Women should be advised that high strength cranberry capsules are more effective than cranberry juice. Flavonoids, which are constituents of cranberries, have an effect on the cytochrome P450 drug-metabolizing enzyme. Flavonoids together with the salicylate content of the juice enhance the anticoagulant effect of coumarins, so concomitant use with warfarin should be avoided.<sup>16</sup> Cranberry juice has also been reported to delay the absorption of Beta-lactam antibiotics.

It is important to point out that both IDSA and Maltese National guidelines do not mention the use of probiotics and cranberry tablets.

### Lifestyle recommendations

Lifestyle changes that will surely help reduce the severity and incidence of cystitis include:

- avoiding perfumed soaps, tight clothing and other potential irritants, such as deodorant sprays
- maintaining good toilet hygiene - wiping from front to back after a bowel movement helps prevent bacteria in the anal region from spreading to the vagina and urethra
- drinking large quantities of water (about 2L a day) so as to flush out the bladder and reduce the acidity of the urine by dilution
- avoiding foods and drinks that contribute to cystitis, examples being alcohol, spices, chocolate, caffeine,

### Key points

- Episodes of cystitis are quite common in females but they are relatively rare in men and children
- A woman is said to have recurrent UTIs if she suffers from three episodes in the past twelve months or two in the previous six months
- Prophylactic antibiotic therapy should be taken at night when the urine flow is low; ideally, it should not be taken for more than six to twelve months
- When possible, urine specimens should be collected before initiating antibiotic therapy so as to avoid interference with laboratory findings

citrus beverages, tomatoes, vitamin C and citrus fruits

- urinating frequently without delay
- not using a spermicide but considering alternative methods of contraception
- taking showers rather than baths
- using tampons for periods
- wearing cotton underwear
- using an oestrogen cream in some postmenopausal women

### Conclusion

Men, children under 16 years of age, pregnant women and individuals suffering from certain conditions that include diabetes, heart and/or renal disease should be immediately referred to a physician if they suffer from symptoms pertaining to cystitis. A specific recommended treatment protocol is not suitable for all countries because the resistance patterns of *Escherichia coli* vary considerably.

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